Amendment and Response Serial No.: 10/580,979

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For: REPLICATION COMPETENT HEPATITIS C VIRUS AND METHODS OF USE

Amendments to the Specification

Please replace the paragraph beginning at page 1, line 20, with the following amended paragraph.

Hepatitis C virus is the most common cause of chronic viral hepatitis within the United States, infecting approximately 4 million Americans and responsible for the deaths of 8,000-10,000 persons annually due to progressive hepatic fibrosis leading to cirrhosis and/or the development of hepatocellular carcinoma. Hepatitis C virus is a single stranded, positive-sense RNA virus with a genome length of approximately 9.6 kb. It is currently classified within a separate genus of the flavivirus family, the genus Hepacivirus. The hepatitis C virus genome contains a single large open reading frame (ORF) that follows a 5' non-translated RNA of approximately 342 bases containing an internal ribosome entry segment (IRES) directing cap-independent initiation of viral translation. The large ORF encodes a polyprotein which undergoes post-translational cleavage, under control of cellular and viral proteinases. This yields a series of structural proteins which include a core or nucleocapsid protein, two envelope glycoproteins, E1 and E2, and at least six nonstructural replicative proteins. These include NS2 (which with the adjacent NS3 sequence demonstrates cis-active metalloproteinase activity at the NS2/NS3 cleavage site), NS3 (a scrine proteinase/NTPase/RNA helicase), NS4A (scrine proteinase accessory factor), NS4B, NS5A, and NS5B (RNA-dependent RNA polymerase).